Computational Anatomy: Simple Statistics on Interesting Spaces

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Motivation

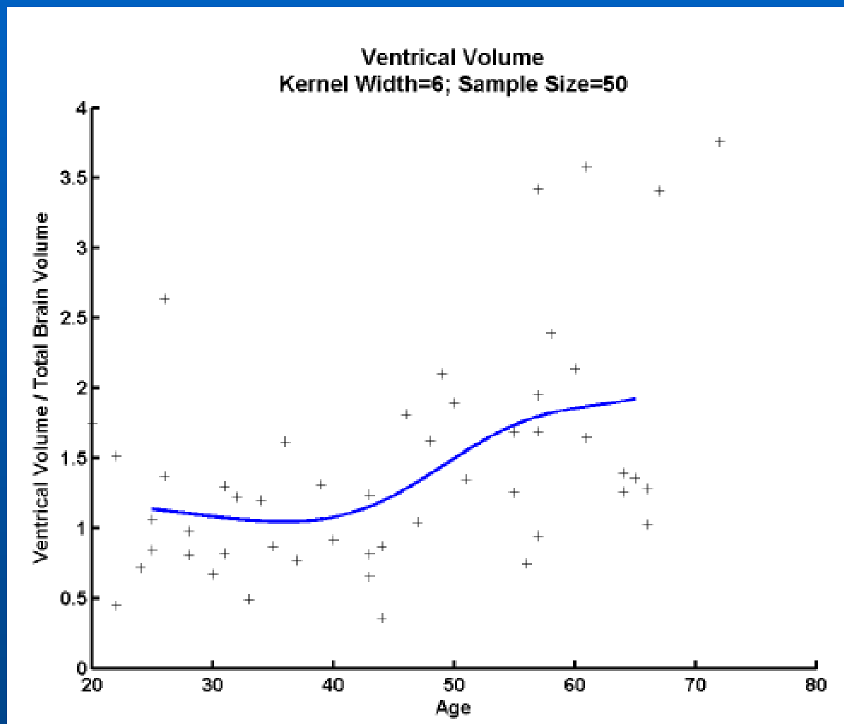
- How can we predict state of dementia from anatomical Images?
- Mathematical formulation:
  - Given a set of training data estimate a function that maps from the Image domain to the various type of outcomes characterizing dementia such as MMSE, CDR and scores of various types of cognition. (A classic regression problem!!)
- Fundamental Statistical problem: High Dimension Low sample size (HDLSS)!!
  - No matter how big the imaging studies (ADNI: approximately 800 subjects) dimension of the the Imaging data much much larger: (256^3 = 16,777,216)!!
  - There is still hope!!
    - Hypothesis: Relevant Inherent dimension of anatomical variation much much smaller!!

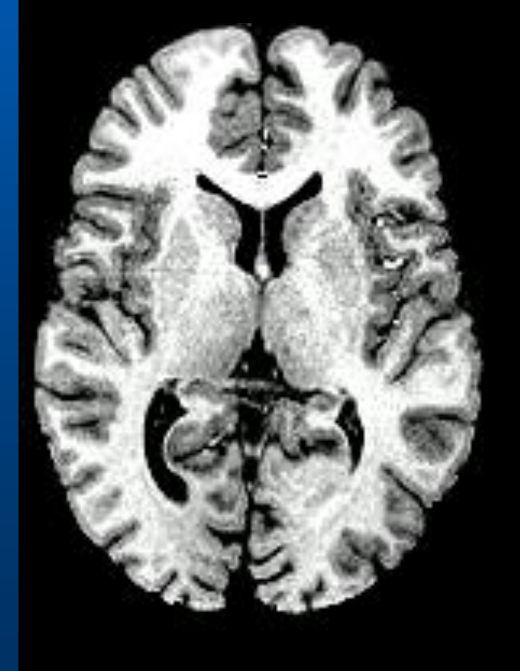
Mathematical Tools Needed

- Fundamental Theoretical Task:
  - Need to generalize High Dimensional Low sample size regression to non-linear space of Anatomical Variation.
- There is Hope:
  - Previously we generalize Standard (Non HDLSS) Kernel Regression to non-linear spaces.
  - Currently working on generalizing Partial Least Squares (PLS) Regression to non-linear spaces.

Previous Work: Regression

- Given an age index population what are the “average” anatomical changes?





B. C. Davis, P. T. Fletcher, E. Bullitt and S. Joshi, "Population Shape Regression From Random Design Data", IEEE International Conference on Computer Vision, *ICCV, 2007. (Winner of David Marr Prize for Best Paper)*

Regression analysis (Review of Kernel Regression)

- Given a set of observation (y_i, t_i) where

$$y(t_i) = m(t_i) + e_i$$

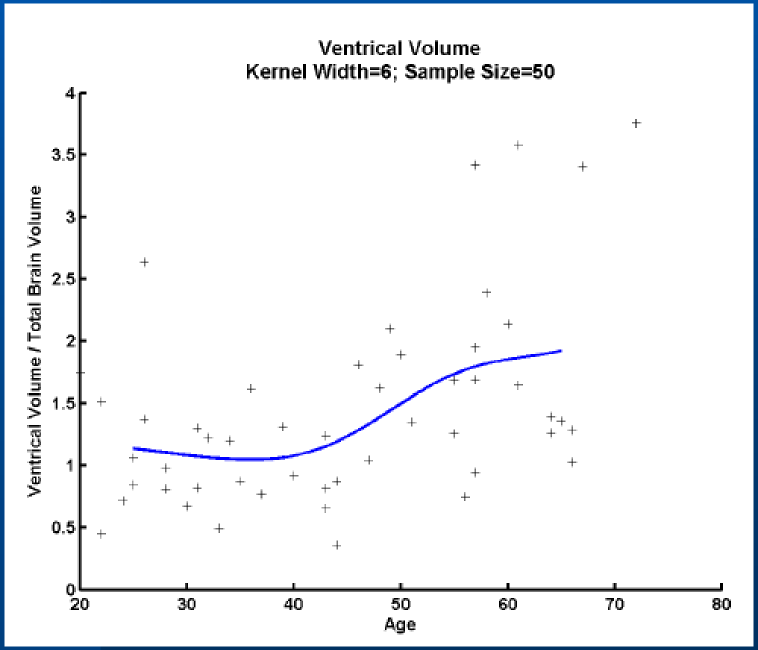
  Estimate function $m(t)$

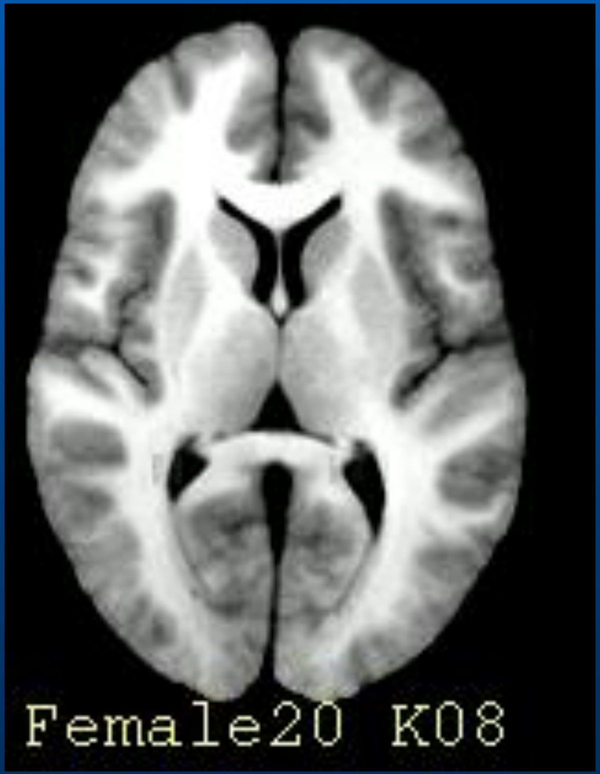
- An estimator is defined as the conditional expectation.
  - Nadaraya-Watson estimator: Moving weighted average, weighted by a kernel.

- Some important observations:
  - No noise in the independent variable t
  - Y can be very high dimensional t is low-dimensional and Euclidian.

Previous Work: Kernel Regression on Riemannien manifolds

- Replace conditional expectation by Fréchet mean!

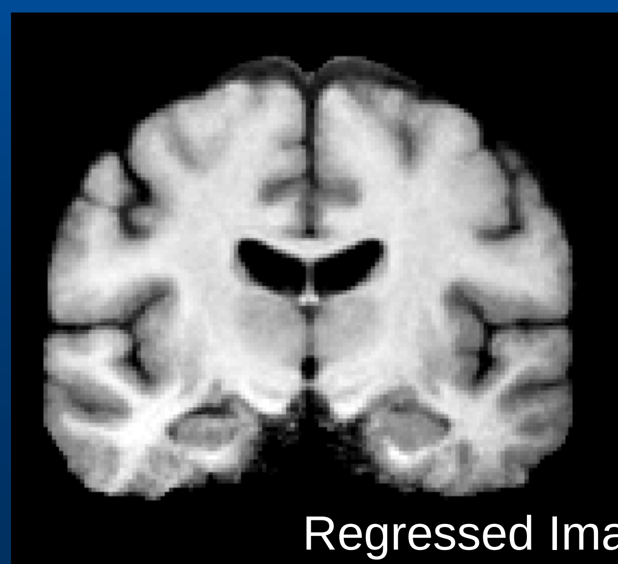
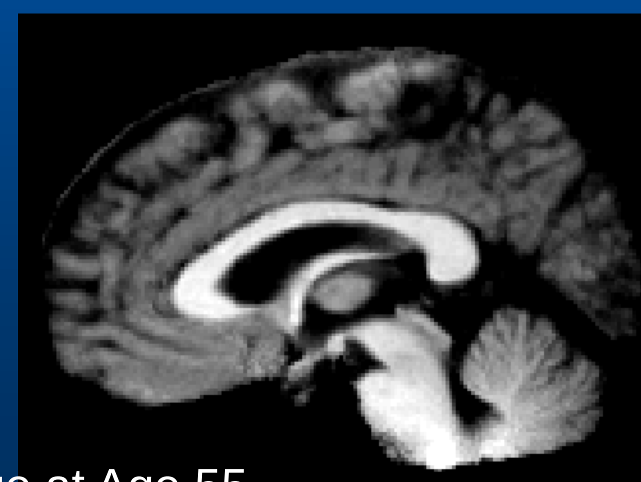




Results

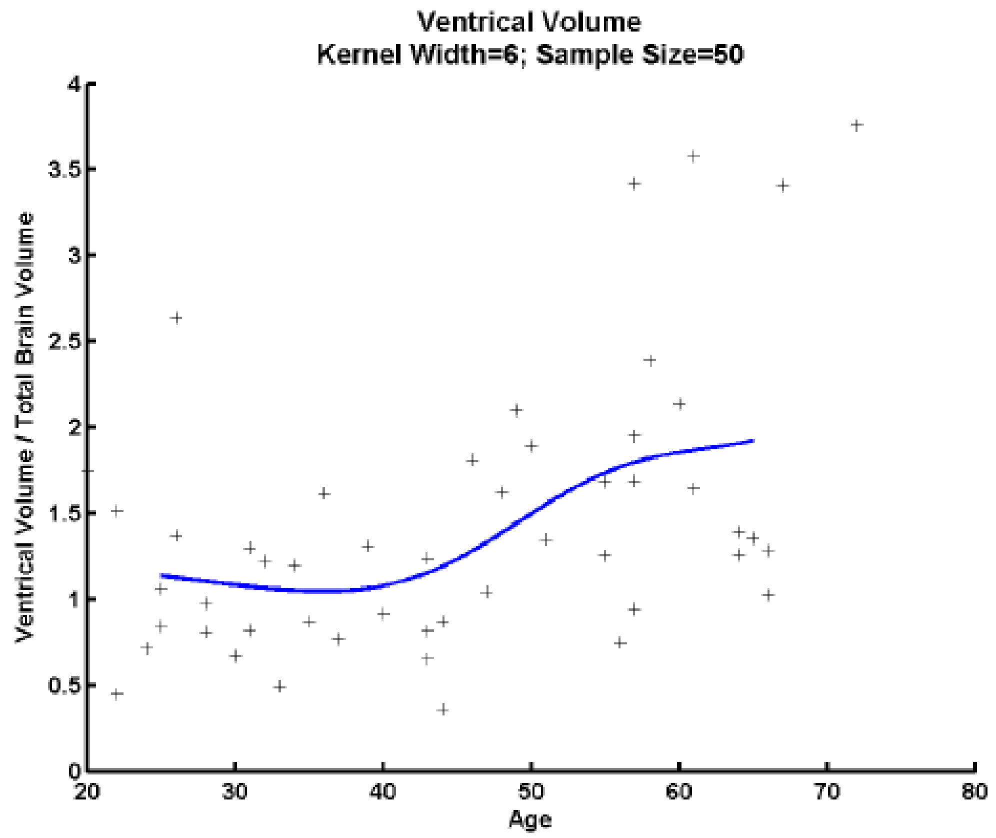


Regressed Image at Age 35

Regressed Image at Age 55

Results



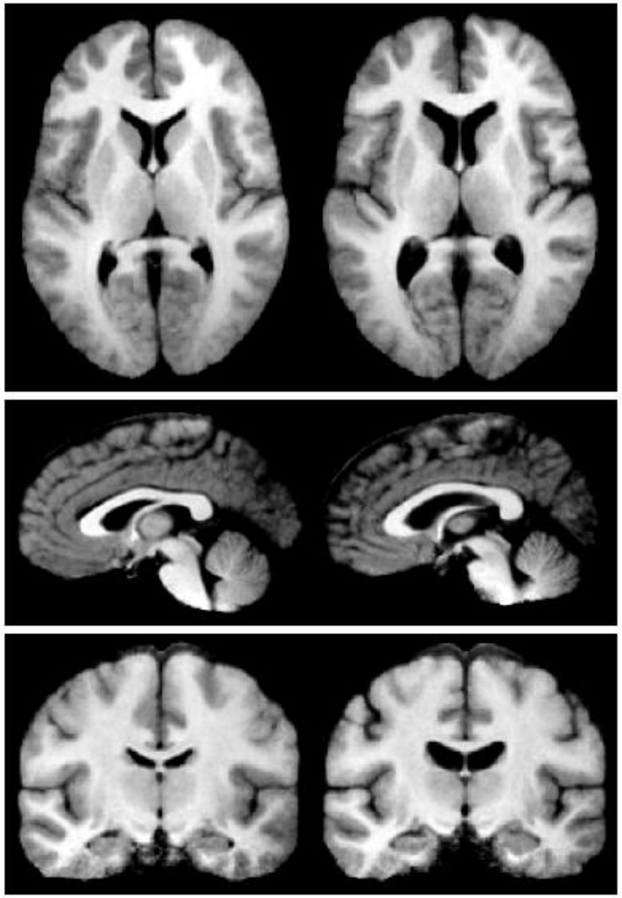
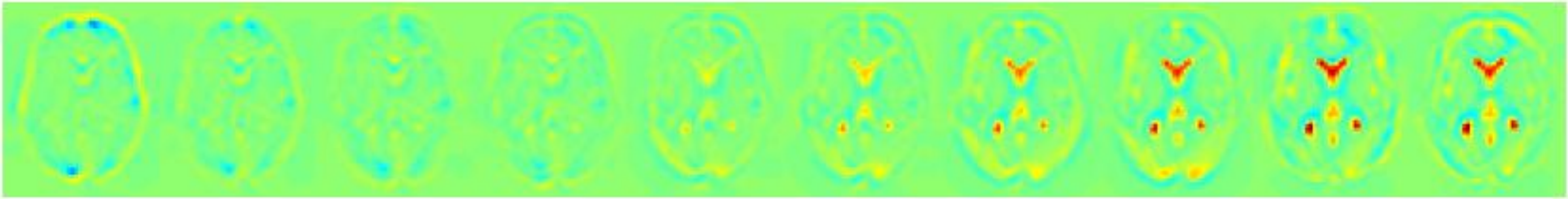


Figure 3. Representative anatomical images for the female cohort at ages 35 (left) and 55 (right). These images were generated from the random design 3D MR database using the shape regression



age=35 37 39 41 43 45 47 49 51 53

Current Work: Extend this to incorporate cognitive measures such as MMSE and CDR

- Fundamental Problems:
  - Cannot just replace MMSE for age or add it as another regressor:
  - MMSE dose not result in Brain changes, the Brain changes impacts MMSE!! (Mike Weiner)
  - MMSE and other scores have inherent nose in the measurements not analogous to age (no noise!!)
  - The anatomical image is the independent variable and the cognitive score is the response!! Hence the HDLSS!!
  - Another major problem: The anatomical variability characterized by a non-linear manifold but hopefully of low inherent dimension.

Current Work: Extend Partial Least Squares (PLS) to Non-linear manifold setting.

- Closely related to principal components regression.
  - In previous work we have extended PCA to principal geodesic analysis:
    - Fletcher PT, Lu C, Pizer SM, Joshi S, Principal geodesic analysis for the study of nonlinear statistics of shape. IEEE Trans Med Imaging 2004 Aug;23(8):995-1005
- PCA regression first finds directions with maximum variance for dimensionality reduction without considering correlation with the response variables.
- PLS regression finds directions considering the covariance between both the variables.
- PLS projects both the observables and the responses.
- PLS very popular in Chemometrics.

PLS continued

- Underlying linear model of PLS both X the predictors and Y the responses have noise, in the linear case the model is given by:

$$\begin{aligned} X &= TP^t + e \\ Y &= TQ^t + e \end{aligned}$$

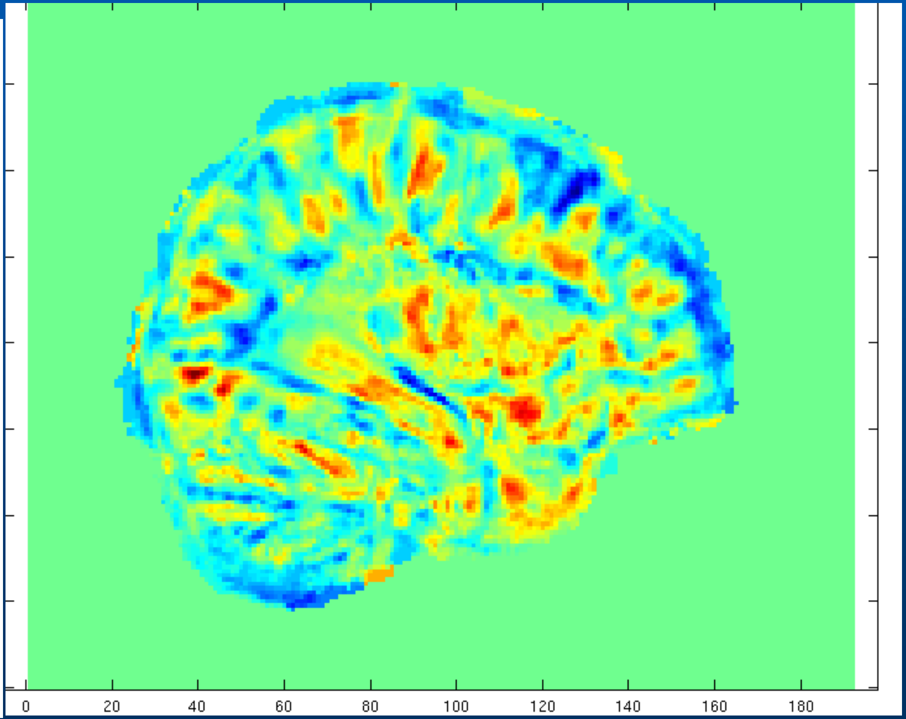
  - Problem: Estimate T the common factors, P and Q the different loadings of the predictors and the responses.

- Final regression is given by a linear function:

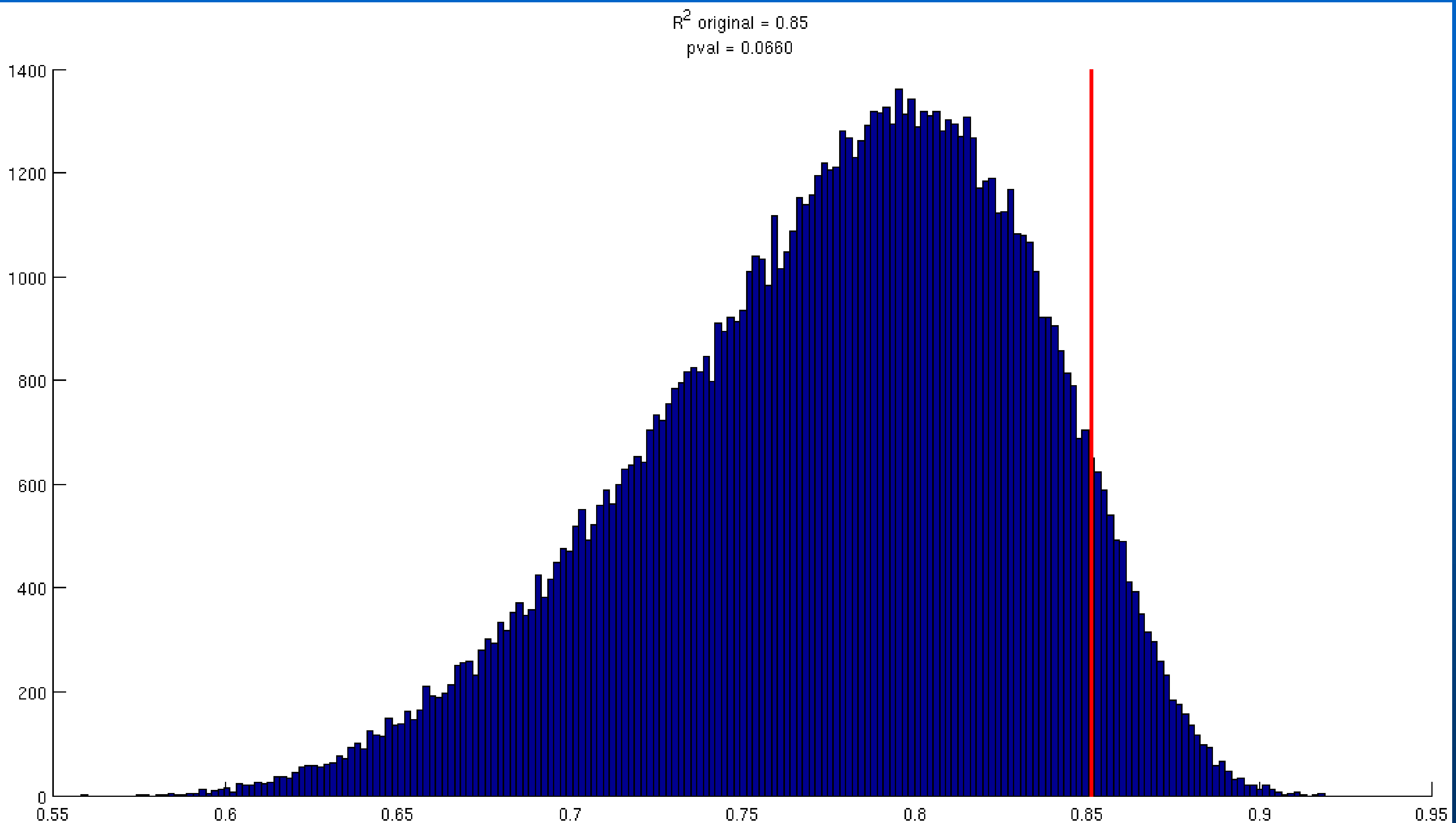
$$Y = B_1 X + B_0$$

PLS: Preliminary Results:

- Performed PLS on MRI intensities of 84 MCI subjects, a subset of the ADNI dataset.
  - Estimated the PLS model with only a single latent dimension.
  - Performed permutation tests to determine the statistical significance of the prediction.



Result of the Permutation Tests: There is Hope!!



Current Work: Extend PLS to non-linear spaces.

- Have some idea how to extend a single factor model.
- Multi factor model not clear, Still brain storming.